UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/045,790	01/14/2002	Richard A. Rosenbloom	QUIG-1006CIP	3053

21302 7590 10/20/2004

KNOBLE, YOSHIDA & DUNLEAVY
EIGHT PENN CENTER
SUITE 1350, 1628 JOHN F KENNEDY BLVD
PHILADELPHIA, PA 19103

EXAMINER	
JIANG, SHAOJIA A	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 10/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/045,790	ROSENBLOOM, RICHARD A.	
	Examiner	Art Unit	
	Shaojia A. Jiang	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 August 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,9-20 and 38-42* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,9-20 and 38-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is a response to Applicant's amendment and response filed on August 2, 2004 wherein claims 1-7 and 9-20 have been amended; claim 8 is cancelled and claims 38-42 are newly submitted. Claims 21-37 are cancelled previously.

Currently, claims 1-7, 9-20, and 38-42 are pending in this application.

Claims 1-7, 9-20, and 38-42 as amended now are examined on the merits herein.

Information Disclosure Statement (IDS)

Applicants' IDS submitted April 9, 2004, June 16 and 24, 2004 is acknowledged. Some non-patent literature documents have been crossed out as they are not appropriate for IDS, i.e., no publication **date**, no name of author and page, are provided.

Applicant's amendment amending claims 1, 7, and 12-19, filed August 2, 2004 with respect to the rejection made under 35 U.S.C. 112 first paragraph for lack of scope of enablement of record stated in the Office Action dated April 9, 2004 has been fully considered and is found persuasive to overcome the rejection since the recitations "one or more compounds effective to regulate at least one of cell differentiation and cell proliferation", "one or more antioxidants" and "anti-inflammatories" have been removed and the particular agents have been recited. Therefore, the said rejection is withdrawn.

Applicant's amendment filed on August 2, 2004 with respect to the rejection of claims 2-3, 7, and 10 made under 35 U.S.C. 112 second paragraph for the use of the

indefinite recitations, i.e., "analogs", "may be", "other", "derivatives" of record stated in the Office Action dated April 9, 2004 have been fully considered and found persuasive to remove the rejection since the indefinite recitations have been deleted from the claims. Therefore, the said rejection is withdrawn.

The terminal disclaimer filed August 2, 2004, disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of U.S. 6,753,325 has been reviewed and is accepted. The terminal disclaimer has been recorded.

The terminal disclaimer filed August 2, 2004, with respect to the rejection of claims 1-9 and 12-20 made under the judicially created doctrine of obviousness-type double patenting as being unpatentable over 1-11 of U.S. Patent 6,753,325 (09/993003) of record in the previous Office Action April 9, 2004, has been considered and found persuasive. Therefore, this obviousness-type double patenting rejection is withdrawn.

The following is new rejection(s) necessitated by Applicant's amendment filed on August 2, 2004, wherein the limitations in the amended claims have been changed.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 4-6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 4 recites the particular antioxidants, "galangin, rutin, luteolin, morin, fisetin, silymarin apigenin, gingkolides, hesperitin, cyanidin, citrin, curcuminoid". There is insufficient antecedent basis for these limitations, since the independent claim 1 which claim 4 is dependent from, does not recite these antioxidants. Note that claim 1 recites "one or more antioxidants selected from the group **consisting of**...." (emphasis added). The transitional phrases "consisting of" employed in the claim is closed-ended and does exclude additional, unrecited elements or method steps. See also MPEP 2111.03. Thus, there is insufficient antecedent basis for this limitation in the claim.

For the same reason, there is insufficient antecedent basis for this limitation in claim 6. Moreover, claim 5 employs the antioxidant "comprises" as transitional phrases. Thus, claim 5 is broader than claim 1 in regard to antioxidants.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 4-9, and 12- 20 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-40 of copending Application No. 10/288,761 for same reasons of record stated in the Office Action dated April 9, 2004.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the copending application is drawn to the same method of the treatment comprising the same active agents as the claims of the instant application. Thus, these methods between in the copending application and in the instant application are seen to substantially overlap.

Thus, the instant claims 1, 4-9, and 12- 20 are seen to be obvious over the claims 1-40 of copending Application No. 10/288,761.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1, 4-9, and 12- 20 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-25 of copending Application No. 10/279,315 for same reasons of record stated in the Office Action dated April 9, 2004.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the copending application is drawn to a method for the

reduction or treatment of reactive and inflammatory dermatoses comprising the same active agents as the claims of the instant application. One of ordinary skill in the art would recognize that radiation injury in a patient would be reactive and inflammatory dermatoses. Thus, these methods between in the copending application and in the instant application are seen to substantially overlap.

Thus, the instant claims 1, 4-9, and 12- 20 are seen to be obvious over the claims 1-25 of copending Application No. 10/279,315.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicant requests deferral of these provisional obviousness-type double patenting rejections until such time as notice of allowance in said co-pending applications are received is noted. Nonetheless, for the reasons of record, said rejections are maintained at this point.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-4, 7, 9-20, 38 and 42 are rejected under 35 U.S.C. 103(a) as being unpatentable over KITA, K (WO 9718817, equivalent to 6,162,801), and Bissett et al. (of

record) and Darr et al. (of record) in view of Shimoi et al. (of record) and Kim et al. (5,776,460, of record).

Kita discloses that vitamin D including vitamin D3 (cholecalciferol), is useful in a dermatological composition for the protection and treatment of the skin and scalp from harmful UV radiation. See 6,162,801, abstract, col.1 lines 22-24 and 51-67, col.4 lines 13-16, and col.8 lines 51 to col. 9.

Bissett et al. discloses that an antioxidant alone such as vitamin C (asorbic acid), or in combination with an anti-inflammatory agent are useful in treating UV radiation-induced chronic skin damage in a mammal. See abstract, page 86 1st paragraph, and Discussion in page 90.

Darr et al. discloses that vitamin C such as asorbic acid or vitamin E is useful in a composition to be administered orally or topically in the treatment of the protection of UV radiation-induced damage. See Summary and page 247.

The prior art does not expressly disclose the employment of the combination of vitamin D3 and ascorbyl palmitate in a composition to be administered in a method for the treatment or reduction of radiation injury. The prior art does also not expressly disclose the composition herein further comprising flavonoid / flavonoid derivatives, and ginseng. The prior art does not expressly disclose that the particular radiation is proton, fluoroscopic, alpha, beta, or gamma radiation.

Shimoi et al. discloses that flavonoid / flavonoid derivatives from plant or tea are antioxidants and have radioprotective effects. See abstract.

Kim et al. discloses that ginseng is known to be useful in the protection of radiation injury. See col.1 lines 21-27.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to employ the combination of vitamin D3 and ascorbyl palmitate in a composition to be administered in a method for the treatment or reduction of radiation injury, and to further comprise flavonoid / flavonoid derivatives, and ginseng in the claimed method.

One having ordinary skill in the art at the time the invention was made would have been motivated to employ the combination of vitamin D3 and ascorbyl palmitate in a composition to be administered in a method for the treatment or reduction of radiation injury since vitamin D such as vitamin D3 is known to be useful for the protection and treatment of the skin and scalp from harmful UV radiation. Antioxidants such as vitamin C (asorbic acid) is known to be useful in the treatment and the protection of UV radiation-induced damage. Moreover, ascorbyl palmitate is a known vitamin C (an ester of asorbic acid). Therefore, one of ordinary skill in the art would have reasonably expected that combining vitamin D3 and ascorbyl palmitate known useful for the same purpose, i.e., treating radiation damage, in a composition to be would improve the therapeutic effect in treating radiation injury.

Further, both flavonoid / flavonoid derivatives and ginseng are known antioxidants and also known to be useful in the protection of radiation injury. Therefore, one of ordinary skill in the art would have reasonably expected that further adding both flavonoid / flavonoid derivatives and ginseng to the composition herein known useful for

the same purpose, in a composition to be administered would provide additive effects for the therapeutic treatment in radiation injury.

Furthermore, one of ordinary skill.in the art would have reasonably expected that the combination herein would also have beneficial therapeutic effects in proton, fluoroscopic, alpha, beta, or gamma radiation.

Since all active composition components herein are known to useful to treat radiation injury, it is considered prima facie obvious to combine them into a single composition to form a third composition useful for the very same purpose. At least additive therapeutic effects would have been reasonably expected. See *In re Kerkhoven*, 205 USPQ 1069 (CCPA 1980).

Thus the claimed invention as a whole is clearly prima facie obvious over the combined teachings of the prior art.

Claims 5-6 and 39-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over KITA, K (WO 9718817, equivalent to 6,162,801), and Bissett et al. (of record) and Darr et al. (of record) in view of Shimoi et al. (of record) and Kim et al. (5,776,460, of record), further in view of Ishida et al. (US 5141741, PTO-892) or Nguyen et al. (US 5650137, PTO-892).

The same disclosures of KITA, K, and Bissett et al. and Darr et al. in view of Shimoi et al. and Kim et al. have been discussed in the 103(a) rejection set forth above.

The prior art does not expressly disclose the employment of the particular antioxidant, alpha.-lipoic acid or chlorophyllin or superoxide dismutase in a composition to be administered in a method for the treatment or reduction of radiation injury.

Ishida et al. discloses that alpha.-lipoic acid and vitamin A, B, C, D, E, F, K, P, U are known to be useful in the protection of UV radiation or anti-sunburn in human skin. See abstract, col.5 lines 65-68.

Nguyen et al. discloses that superoxide dismutase or the porphyrins such as chlorophyllin, alone or in combination are antioxidants and have protective effects to human skin including against UV radiation. See abstract, col.1, col.2 lines 20-31, col.3 lines 40-66, claims 1-11.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to employ the particular antioxidant, alpha.-lipoic acid or chlorophyllin or superoxide dismutase in a composition to be administered in a method for the treatment or reduction of radiation injury.

One having ordinary skill in the art at the time the invention was made would have been motivated to employ the particular antioxidant, alpha.-lipoic acid or chlorophyllin or superoxide dismutase in a composition to be administered in a method for the treatment or reduction of radiation injury, since alpha.-lipoic acid or chlorophyllin or superoxide dismutase, alone or their combination is well known to be useful for the protection and treatment of the skin and scalp from harmful UV radiation, as those known antioxidants taught by the cited prior art.

Therefore, one of ordinary skill in the art would have reasonably expected that alpha.-lipoic acid or chlorophyllin or superoxide dismutase, alone or their combination would have the same usefulness and provide additive effects for the therapeutic treatment in radiation injury. See *In re Kerkhoven*, 205 USPQ 1069 (CCPA 1980).

Response to Argument

Applicant's arguments filed August 2, 2004 with respect to the rejection of claims 1-20 made under 35 U.S.C. 103(a) as being unpatentable over KITA, K (WO 9718817, equivalent to 6,162,801), and Bissett et al. (of record) and Darr et al. (of record) in view of Shimoi et al. (of record) and Kim et al. (5,776,460, of record)have been fully considered but are not deemed persuasive as to the nonobviousness of the claimed invention over the prior art as further discussed below.

Again, Applicant asserts that Kita dose not teach a vitamin D to be administered orally in the claimed method herein in treating radiation injury in a human. Contrary to Applicant's assertion, Kita teaches that "Therapeutic vitamin D is administered orally or by injection, and is applied to the skin as an active vitamin D ointment in the case of skin conditions" (see col.1 lines 42-44 in particular). Kita further teaches that "It is known that the molecular structure of vitamin D is altered in the liver and kidneys, converting it into biologically active vitamin D" (see col.1 lines 44-46 in particular), and "It is now known that there are active vitamin D receptors in the cells, and the inhibition of cell activity is being studied since active vitamin D inhibits the production of a variety of cytokines" (see col.1 lines 63-67). Moreover, Kita teaches that "In general, the ultraviolet

(UV) light absorption spectra of vitamin D and active vitamin D have absorption maxima 265 nm, with the molar absorption coefficients of about 18,000". See col.1 lines 25-28. Hence, one of skill in the art would recognize that the molar absorption coefficients of UV radiation for vitamin D are very high. Therefore, based on the teachings of Kita, one of ordinary skill in the art would have found it obvious to administer a vitamin D orally in treating radiation injury in a human.

Additionally, oral administrations of vitamin D or D3 are well-known in the art. Applicant's argument in regard to inherency of oral administration of vitamin D has been considered. Note that the rejection herein is made under 35 U.S.C. 103(a) not 102(b). Thus, the inherency rationale is not applied herein.

Furthermore, as indicated in the previous Office Action, since all active composition components herein are known to useful to treat radiation injury, it is considered prima facie obvious to combine them into a single composition to form a third composition useful for the very same purpose. At least additive therapeutic effects would have been reasonably expected. See *In re Kerkhoven*, 205 USPQ 1069 (CCPA 1980).

It is noted that the record contains no clear and convincing evidence of nonobviousness or **unexpected results** for the oral compositions herein employed in the claimed method herein over the prior art.

For the above stated reasons, said claims are properly rejected under 35 U.S.C. 103(a). Therefore, said rejection is adhered to.

In view of the rejections to the pending claims set forth above, no claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Jiang, whose telephone number is (571)272-0627. The examiner can normally be reached on Monday-Friday from 9:00 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, Ph.D., can be reached on (571)272-0629. The fax phone number for the organization where this application or proceeding is assigned is 703.872.9307.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

S. Anna Jiang, Ph.D.
Primary Examiner, AU 1617
October 12, 2004